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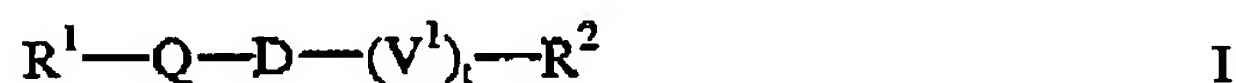
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AMENDMENTS TO THE CLAIMS

The following listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of claims:

1 (currently amended). A compound of Formula I



or a pharmaceutically acceptable salt thereof,
wherein:

R^1 and R^2 independently are selected from:

- C₁-C₆ alkyl;
- Substituted C₁-C₆ alkyl;
- C₂-C₆ alkenyl;
- Substituted C₂-C₆ alkenyl;
- C₂-C₆ alkynyl;
- Substituted C₂-C₆ alkynyl;
- C₃-C₆ cycloalkyl;
- Substituted C₃-C₆ cycloalkyl;
- C₃-C₆ cycloalkyl-(C₁-C₆ alkylenyl);
- Substituted C₃-C₆ cycloalkyl-(C₁-C₆ alkylenyl);
- 3- to 6-membered heterocycloalkyl;
- Substituted 3- to 6-membered heterocycloalkyl;
- 3- to 6-membered heterocycloalkyl-(C₁-C₆ alkylenyl);
- Substituted 3- to 6-membered heterocycloalkyl-(C₁-C₆ alkylenyl);
- Phenyl-(C₁-C₆ alkylenyl);
- Substituted phenyl-(C₁-C₆ alkylenyl);
- Naphthyl-(C₁-C₆ alkylenyl);
- Substituted naphthyl-(C₁-C₆ alkylenyl);
- 5-, 6-, 9-, and 10-membered heteroaryl-(C₁-C₆ alkylenyl);

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Substituted 5-, 6-, 9-, and 10-membered heteroaryl-(C₁-C₆ alkylenyl);

Phenyl;

Substituted phenyl;

Naphthyl;

Substituted naphthyl;

5-, 6-, 9-, and 10-membered heteroaryl;

Substituted 5-, 6-, 9-, and 10-membered heteroaryl;

R³O-(C₁-C₆ alkylenyl);

Substituted R³O-(C₁-C₆ alkylenyl);

Phenyl-O-(C₁-C₈ alkylenyl);

Substituted phenyl-O-(C₁-C₈ alkylenyl);

Phenyl-S-(C₁-C₈ alkylenyl);

Substituted phenyl-S-(C₁-C₈ alkylenyl);

Phenyl-S(O)-(C₁-C₈ alkylenyl);

Substituted phenyl-S(O)-(C₁-C₈ alkylenyl);

Phenyl-S(O)₂-(C₁-C₈ alkylenyl); and

Substituted phenyl-S(O)₂-(C₁-C₈ alkylenyl);

wherein R¹ and R² are not both selected from:

C₁-C₆ alkyl;

C₂-C₆ alkenyl;

C₂-C₆ alkynyl; and

C₃-C₆ cycloalkyl;

Each R³ independently is selected from:

H;

C₁-C₆ alkyl;

Substituted C₁-C₆ alkyl;

C₃-C₆ cycloalkyl;

Substituted C₃-C₆ cycloalkyl;

Phenyl-(C₁-C₆ alkylenyl);

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Substituted phenyl-(C₁-C₆ alkylenyl);Naphthyl-(C₁-C₆ alkylenyl);Substituted naphthyl-(C₁-C₆ alkylenyl);5-, 6-, 9-, and 10-membered heteroaryl-(C₁-C₆ alkylenyl);Substituted 5-, 6-, 9-, and 10-membered heteroaryl-(C₁-C₆ alkylenyl);

Phenyl;

Substituted phenyl;

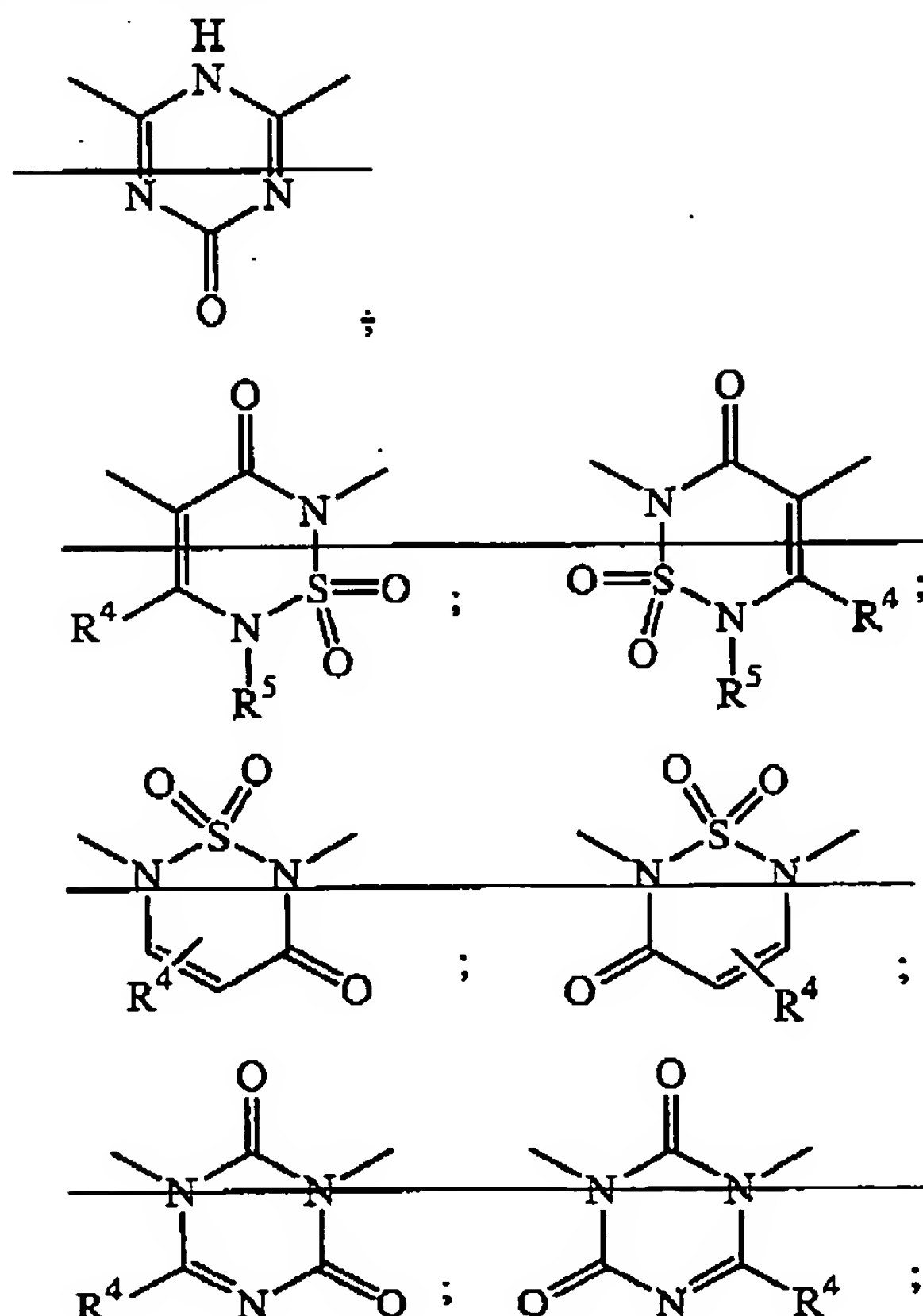
Naphthyl;

Substituted naphthyl;

5-, 6-, 9-, and 10-membered heteroaryl;

Substituted 5-, 6-, 9-, and 10-membered heteroaryl;

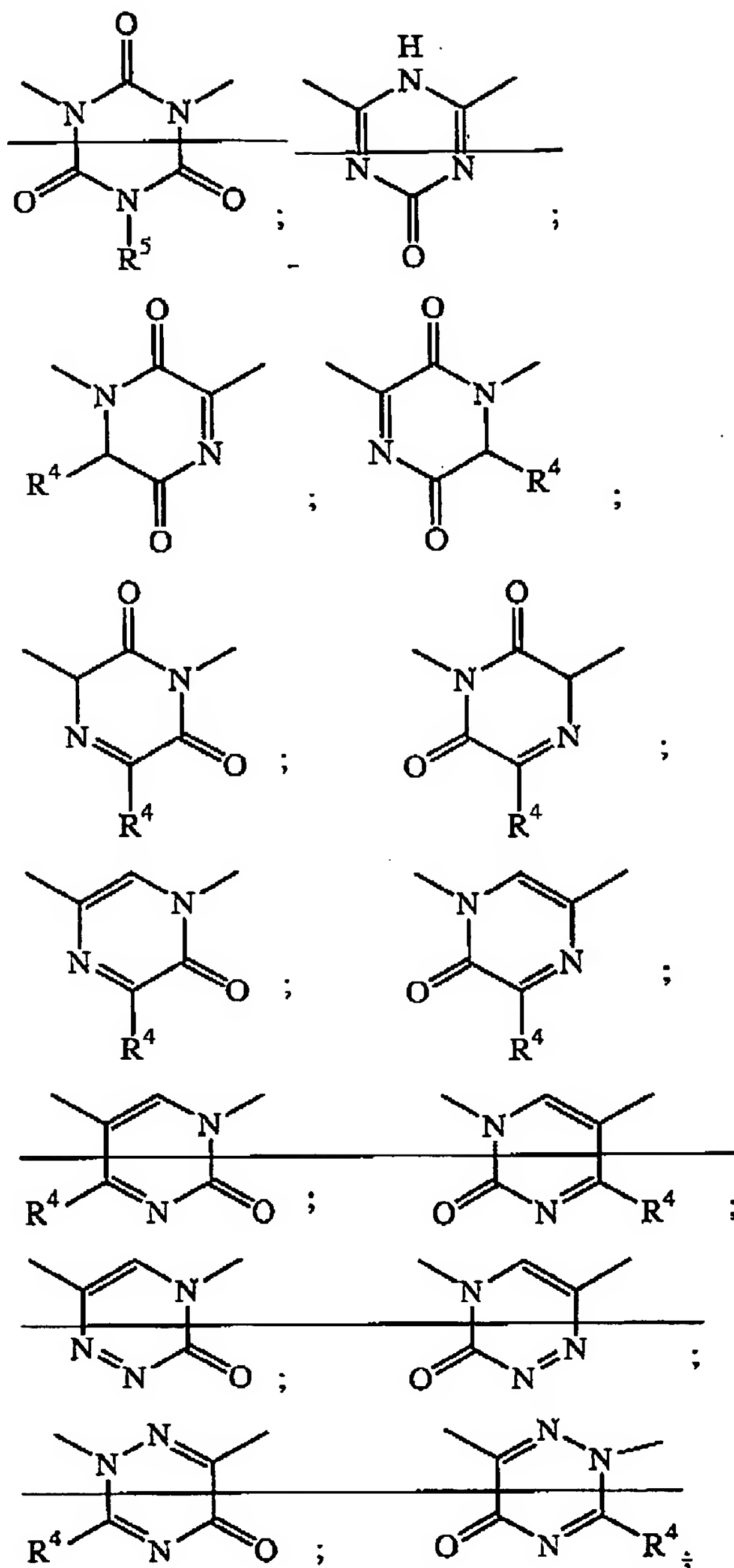
D is a heteromonocyclic diradical:



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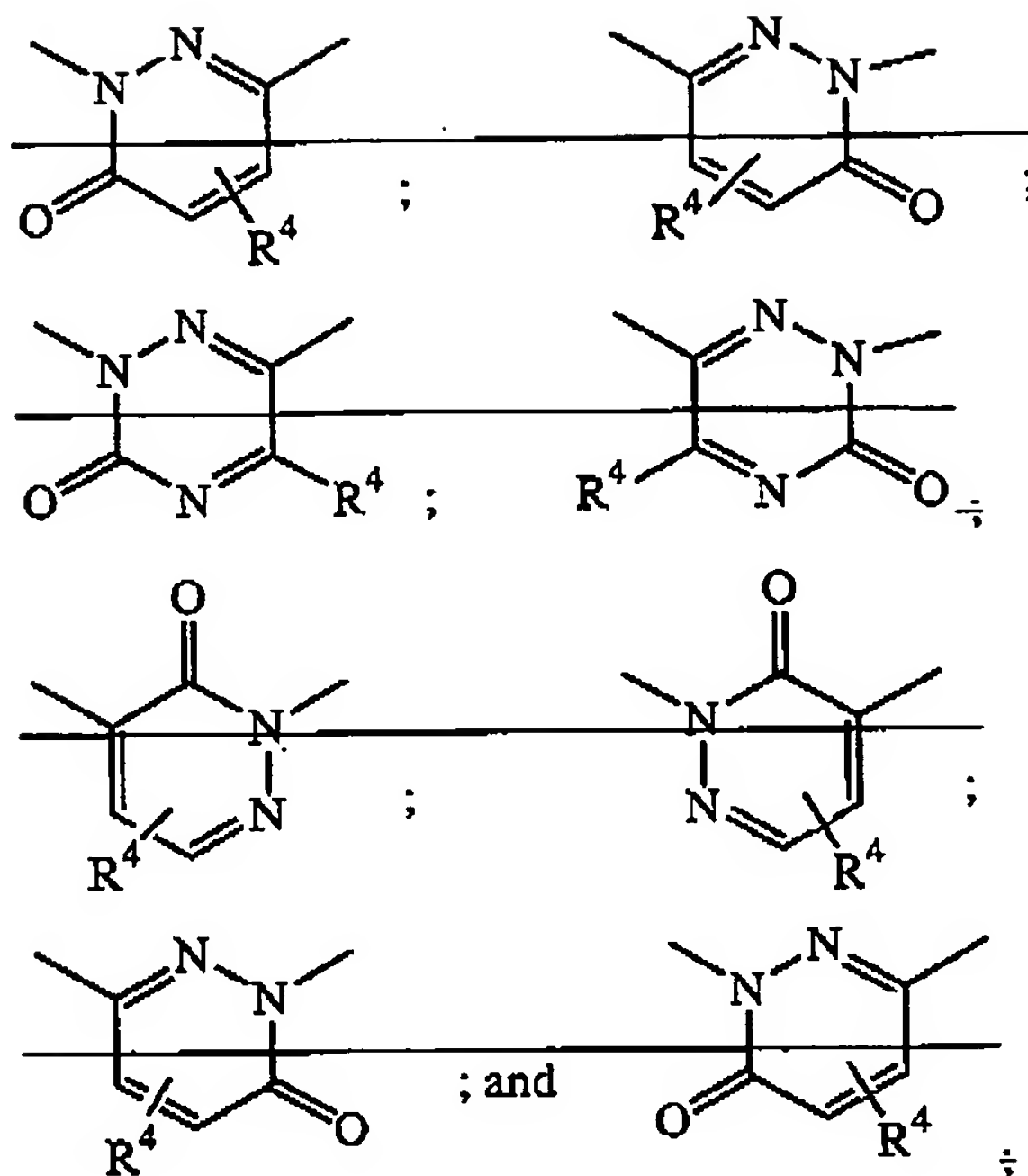
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Each R^4 independently is selected from:

H;
 F;
 CH₃;
 CF₃;
 C(O)H;
 CN;
 HO;
 CH₃O;
 C(F)H₂O;
 C(H)F₂O; and
 CF₃O;

t is an integer of 0 or 1;

V^1 is selected from:

a 5-membered heteroarylenyl;

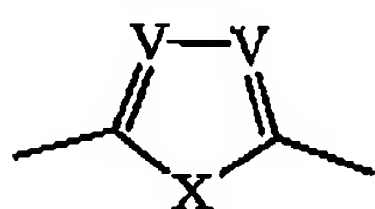
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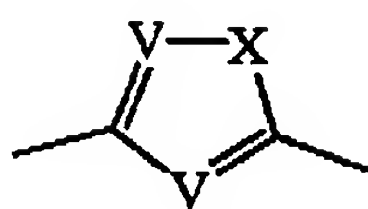
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 $\text{CH}_2\text{C}\equiv\text{C};$ $\text{CF}_2\text{C}\equiv\text{C};$ $\text{C}(\text{O})\text{O};$ $\text{C}(\text{S})\text{O};$ $\text{C}(\text{O})\text{N}(\text{R}^5);$ and $\text{C}(\text{S})\text{N}(\text{R}^5);$

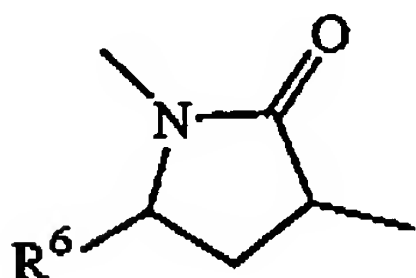
Q, when bonded to a nitrogen atom in group D, is selected from:

 $\text{OC}(\text{O});$ $\text{CH}(\text{R}^6)\text{C}(\text{O});$ $\text{OC}(\text{NR}^6);$ $\text{CH}(\text{R}^6)\text{C}(\text{NR}^6);$ $\text{N}(\text{R}^6)\text{C}(\text{O});$ $\text{N}(\text{R}^6)\text{C}(\text{S});$ $\text{N}(\text{R}^6)\text{C}(\text{NR}^6);$ $\text{SC}(\text{O});$ $\text{CH}(\text{R}^6)\text{C}(\text{S});$ $\text{SC}(\text{NR}^6);$ $\text{C}\equiv\text{CCH}_2;$ $\text{C}\equiv\text{CCF}_2;$ 

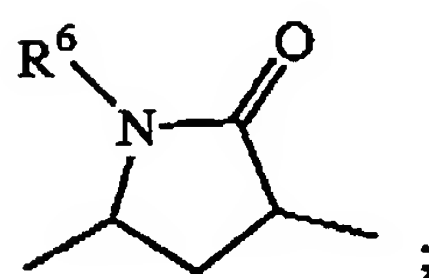
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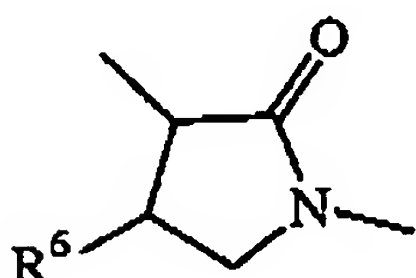
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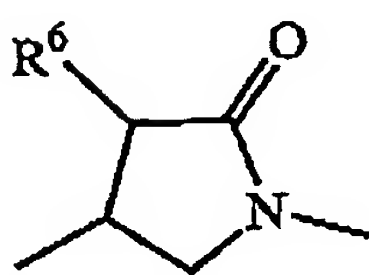
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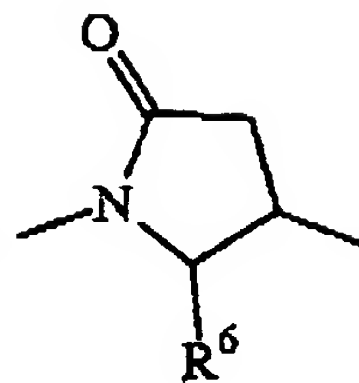
;



;



; and



; and

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Q, when bonded to a carbon atom in group D, is as defined above and may further be selected from:

OCH_2 ;

$\text{N(R}^6\text{)CH}_2$;

trans-(H)C=C(H) ;

cis-(H)C=C(H) ;

$\text{C}\equiv\text{C}$;

$\text{CH}_2\text{C}\equiv\text{C}$; and

$\text{CF}_2\text{C}\equiv\text{C}$;

Each X independently is O, S, N(H), or N(C₁-C₆ alkyl);

Each V independently is C(H) or N;

Each R⁵ independently is H or C₁-C₆ alkyl;

R⁶ is H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl; 3- to 6-membered heterocycloalkyl;

phenyl; benzyl; or 5- or 6-membered heteroaryl;

Each "substituted" group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

C₁-C₆ alkyl;

C₂-C₆ alkenyl;

C₂-C₆ alkynyl;

C₃-C₆ cycloalkyl;

C₃-C₆ cycloalkylmethyl;

Phenyl;

Phenylmethyl;

3- to 6-membered heterocycloalkyl;

3- to 6-membered heterocycloalkylmethyl;

cyano;

CF₃;

(C₁-C₆ alkyl)-OC(O);

HOCH₂;

(C₁-C₆ alkyl)-OCH₂;

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H₂NCH₂;
(C₁-C₆ alkyl)-N(H)CH₂;
(C₁-C₆ alkyl)₂-NCH₂;
N(H)₂C(O);
(C₁-C₆ alkyl)-N(H)C(O);
(C₁-C₆ alkyl)₂-NC(O);
N(H)₂C(O)N(H);
(C₁-C₆ alkyl)-N(H)C(O)N(H);
N(H)₂C(O)N(C₁-C₆ alkyl);
(C₁-C₆ alkyl)-N(H)C(O)N(C₁-C₆ alkyl);
(C₁-C₆ alkyl)₂-NC(O)N(H);
(C₁-C₆ alkyl)₂-NC(O)N(C₁-C₆ alkyl);
N(H)₂C(O)O;
(C₁-C₆ alkyl)-N(H)C(O)O;
(C₁-C₆ alkyl)₂-NC(O)O;
HO;
(C₁-C₆ alkyl)-O;
CF₃O;
CF₂(H)O;
CF(H)₂O;
H₂N;
(C₁-C₆ alkyl)-N(H);
(C₁-C₆ alkyl)₂-N;
O₂N;
(C₁-C₆ alkyl)-S;
(C₁-C₆ alkyl)-S(O);
(C₁-C₆ alkyl)-S(O)₂;
(C₁-C₆ alkyl)₂-NS(O)₂;
(C₁-C₆ alkyl)-S(O)₂-N(H)-C(O)-(C₁-C₈ alkylene)_m; and
(C₁-C₆ alkyl)-C(O)-N(H)-S(O)₂-(C₁-C₈ alkylene)_m;

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wherein each substituent on a carbon atom may further be independently selected from:

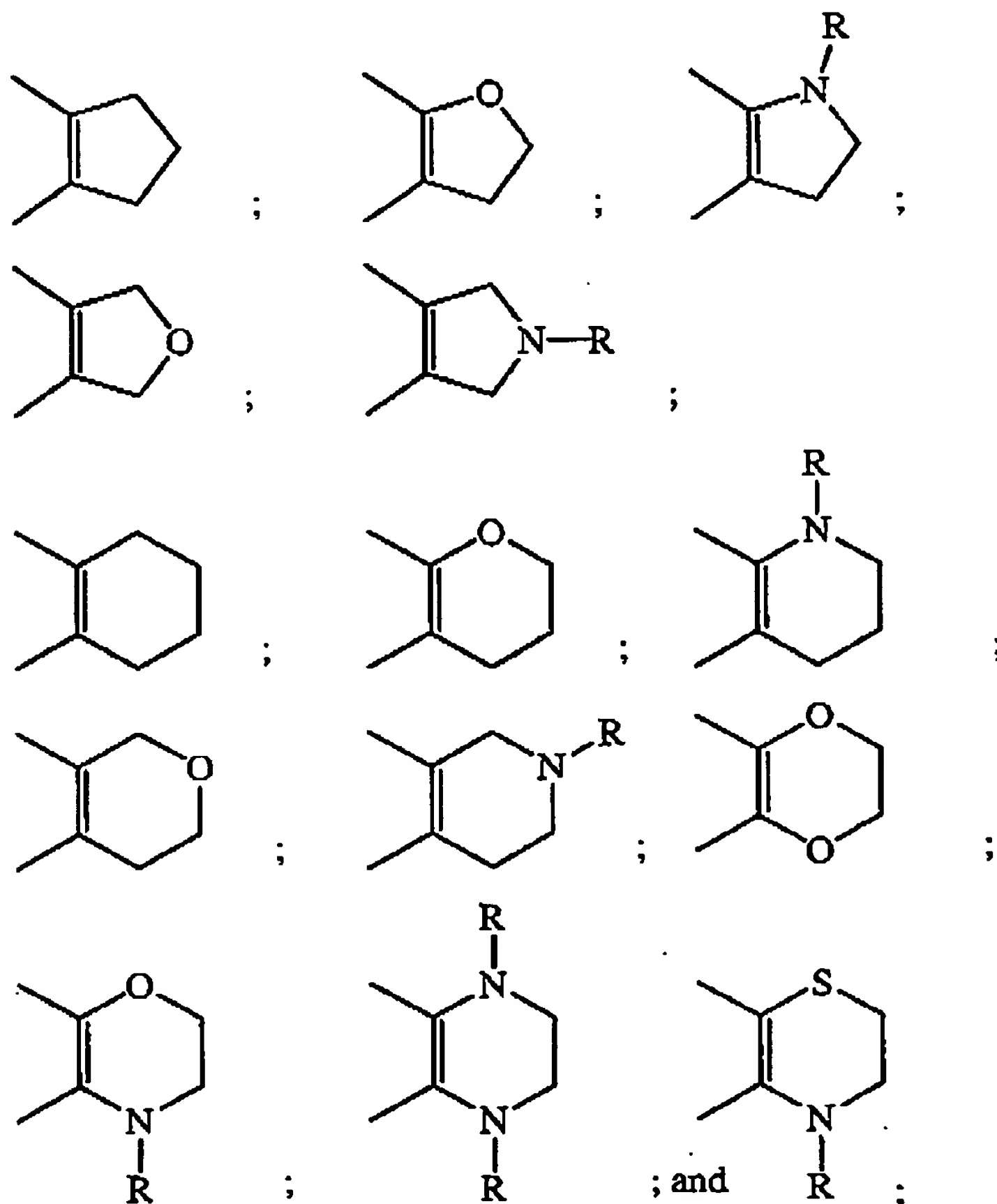
Halo;

HO₂C; and

OCH₂O, wherein each O is bonded to adjacent carbon atoms to form a 5-membered ring;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

wherein two adjacent, substantially sp² carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:



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R is H or C₁-C₆ alkyl;

wherein each 5-membered heteroarylenyl independently is a 5-membered ring containing carbon atoms and from 1 to 4 heteroatoms selected from 1 O, 1 S, 1 NH, 1 N(C₁-C₆ alkyl), and 4 N, wherein the O and S atoms are not both present, and wherein the heteroarylenyl may optionally be unsubstituted or substituted with 1 substituent selected from fluoro, methyl, hydroxy, trifluoromethyl, cyano, and acetyl;

wherein each heterocycloalkyl is a ring that contains carbon atoms and 1 or 2 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)₂, 1 N, 2 N(H), and 2 N(C₁-C₆ alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C₁-C₆ alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms and 1 or 2 heteroatoms independently selected from N, N(H), and N(C₁-C₆ alkyl), and 5- and 6-membered heteroaryl are monocyclic rings; and 9- and 10-membered heteroaryl are 6,5-fused and 6,6-fused bicyclic rings, respectively, wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other;

wherein with any (C₁-C₆ alkyl)₂-N group, the C₁-C₆ alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and

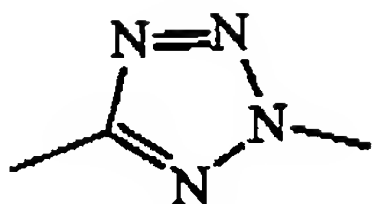
wherein each group and each substituent recited above is independently selected.

2 (original). The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein V¹ is

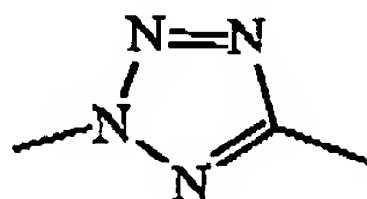
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3 (original). The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein V^1 is



4 (original). The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is $N(R^6)C(O)$.

5 (original). The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is $C\equiv C$.

6 (original). The compound according to any one of Claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein at least one of R^1 and R^2 is independently selected from:

Phenyl-(C_1 - C_6 alkylenyl); and

Substituted phenyl-(C_1 - C_6 alkylenyl);

wherein each group and each substituent is independently selected.

7 (original). The compound according to any one of Claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein at least one of R^1 and R^2 is independently selected from:

5-, 6-, 9-, and 10-membered heteroaryl-(C_1 - C_6 alkylenyl); and

Substituted 5-, 6-, 9-, and 10-membered heteroaryl-(C_1 - C_6 alkylenyl);

wherein each heteroaryl contains carbon atoms and from 1 to 4 heteroatoms

independently selected from 1 O, 1 S, 1 N(H), 1 N(C_1 - C_6 alkyl), and 4 N,

and 5- and 6-membered heteroaryl are monocyclic rings and 9- and 10-

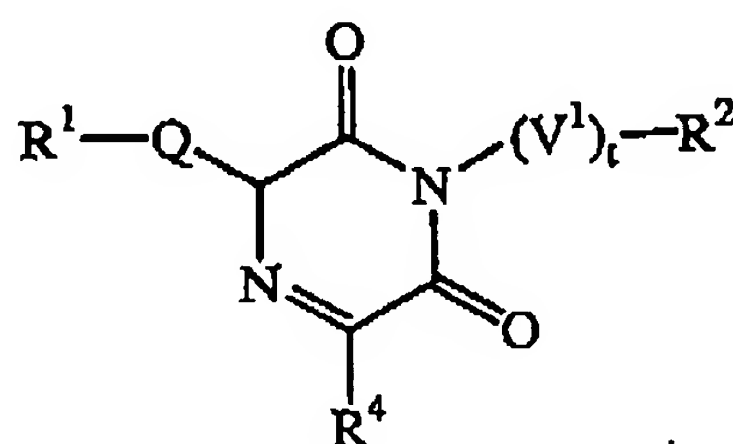
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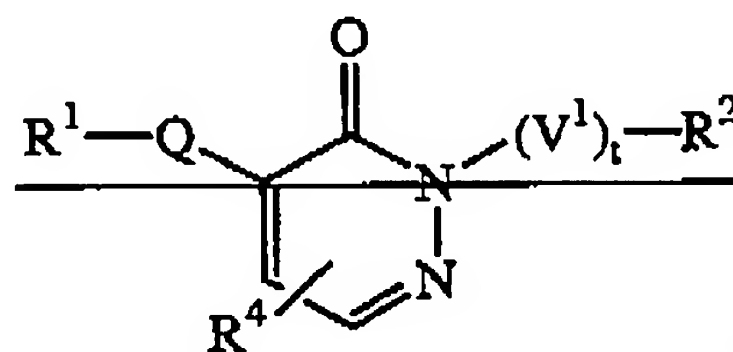
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membered heteroaryl are 6,5-fused and 6,6-fused bicyclic rings, respectively, wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other; and wherein each group and each substituent is independently selected.

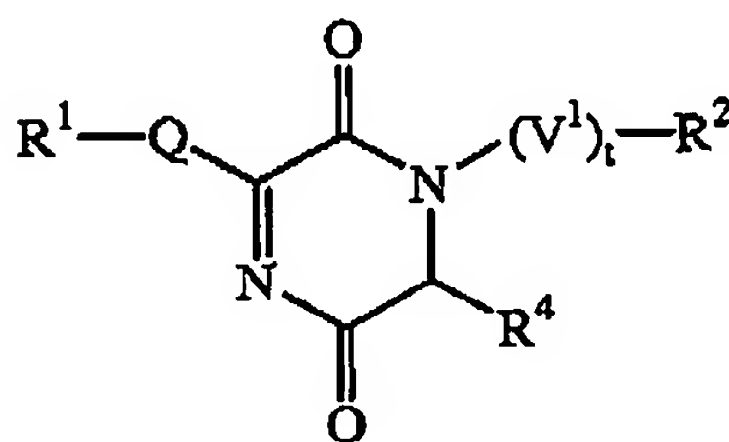
8 (currently amended). A compound of Formula ~~II, III, IV, V, or VI~~ II or IV



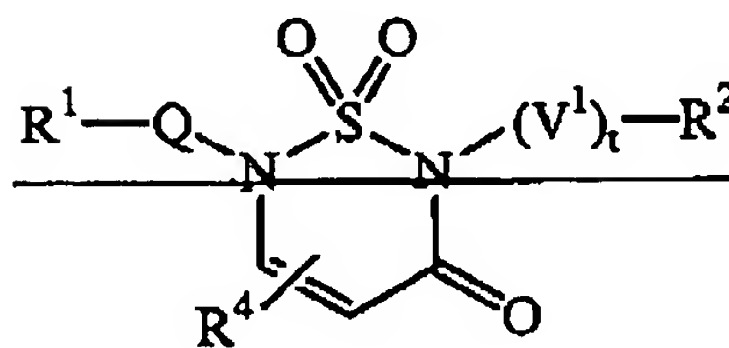
II



III



IV

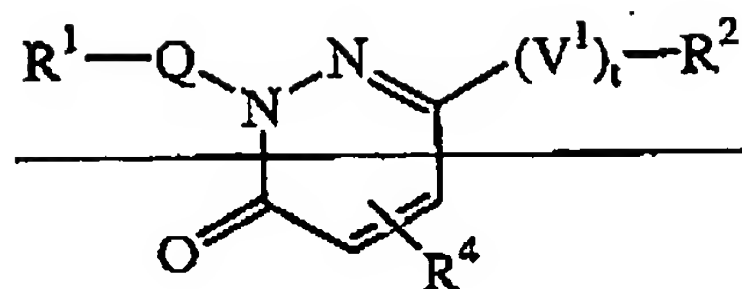


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and

VI

or a pharmaceutically acceptable salt thereof.

- 9 (original). The compound of Formula II according to Claim 8, selected from:
- 4-[5-(3-Benzylcarbonyl-2,6-dioxo-3,6-dihydro-2H-pyrazin-1-yl)-tetrazol-2-yl]-benzoic acid;
 - 4-(5-{2,6-Dioxo-3-[(pyridin-4-ylmethyl)-carbonyl]-3,6-dihydro-2H-pyrazin-1-yl}-tetrazol-2-yl)-benzoic acid;
 - 4-[3-(3-Benzylcarbonyl-2,6-dioxo-3,6-dihydro-2H-pyrazin-1-yl)-prop-2-ynyl]-benzoic acid;
 - 4-(3-{2,6-Dioxo-3-[(pyridin-4-ylmethyl)-carbonyl]-3,6-dihydro-2H-pyrazin-1-yl}-prop-2-ynyl)-benzoic acid;
 - 4-{2-[2,6-Dioxo-3-(3-phenyl-prop-1-ynyl)-3,6-dihydro-2H-pyrazin-1-yl]-oxazol-5-yl}-benzoic acid;
 - 4-{2-[3-(3-Imidazol-1-yl-prop-1-ynyl)-2,6-dioxo-3,6-dihydro-2H-pyrazin-1-yl]-oxazol-4-yl}-benzoic acid;
 - 4-{3-[2,6-Dioxo-3-(3-phenyl-prop-1-ynyl)-3,6-dihydro-2H-pyrazin-1-yl]-prop-2-ynyl}-benzoic acid;
 - 4-{3-[3-(3-Imidazol-1-yl-prop-1-ynyl)-2,6-dioxo-3,6-dihydro-2H-pyrazin-1-yl]-prop-2-ynyl}-benzoic acid;
 - 4-({[2,6-Dioxo-3-(5-phenyl-oxazol-2-yl)-3,6-dihydro-2H-pyrazine-1-carbonyl]-amino}-methyl)-benzoic acid;
 - 4-{3-[2,6-Dioxo-3-(5-phenyl-oxazol-2-yl)-3,6-dihydro-2H-pyrazin-1-yl]-prop-2-ynyl}-benzoic acid;
 - 4-{5-[2,6-Dioxo-3-(4-phenyl-oxazol-2-yl)-3,6-dihydro-2H-pyrazin-1-yl]-tetrazol-2-yl}-benzoic acid; and

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4-{3-[2,6-Dioxo-3-(4-phenyl-oxazol-2-yl)-3,6-dihydro-2H-pyrazin-1-yl]-
prop-2-ynyl}-benzoic acid;
or a pharmaceutically acceptable salt thereof.

10 (canceled).

11 (original). A pharmaceutical composition, comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

12 (canceled).

13 (original). A method for treating osteoarthritis or rheumatoid arthritis, comprising administering to a patient suffering from osteoarthritis or rheumatoid arthritis a nontoxic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

14 (canceled).